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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/721,543	11/21/2000	Fenyong Liu	BERK-005	2657

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EXAMINER	
NGUYEN, QUANG	
ART UNIT	PAPER NUMBER
1636	9

DATE MAILED: 06/19/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Offic Action Summary	Application N .	Applicant(s)	
	09/721,543	LIU ET AL.	
	Examiner	Art Unit	
	Quang Nguyen, Ph.D	1636	

-- The MAILING DATE of this communication appears n the cover she t with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 April 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disp sition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) *9,11,22 and 24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,10,12-21,23,25 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5,8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicants' amendment filed April 17, 2002 in Paper No. 7 has been entered. Claims 1-26 are pending in the present application.

Applicants elected with traverse the polynucleotide sequences in Group 3 (SEQ ID NOs. 12-16) as a separate invention. Applicants mainly argued the class of antiviral agents represent a generic claim, and that the election of SEQ ID NOs: 12-16 should be an election of species in the group, not a separate invention, because the family of antiviral agents set forth in the claims have a common mechanism of function, through binding to virus and acting to decrease the infection of target cells by the virus. Applicants' arguments are respectfully found to be unpersuasive for the following reasons.

Claims 1-8, 12-21 and 25-26 link a plurality of patentably distinct groups of polynucleotide ligand sequences having antiviral activity that lack the unity of invention. As set forth in MPEP 803.02, unity of invention exists if all species recited in a claim (1) shows a common utility, and (2) share a substantial structural feature disclosed as being essential to that utility. Claims 1-8, 12-21 and 25-26 do not have unity of the invention because a plurality of disclosed patentably distinct groups of polynucleotide ligand sequences having no substantial common structural features. Moreover, the distinct groups of polynucleotide ligand sequences do not necessarily bind to the same viral protein and therefore acting to decrease the infection of the virus to a cell. Thus, claims 1-8, 12-21 and 25-26 are improper written as linking or Markush claims linking multiple distinct inventions. Additionally, because of limited resources from the US PTO

to conduct the computer search for all the claimed SEQ ID NOs, an undue burden would be needed to search and examine all the claimed inventions in a single application. Therefore, restriction for examination purposes as indicated is proper.

The requirement is still deemed proper and is therefore made **FINAL**.

Claims 9, 11, 22 and 24 are withdrawn from further consideration because they are drawn to non-elected inventions.

Claims 1-8, 10, 12-21, 23, 25-26 are examined on the merits herein.

Specification

In the Brief Description of the Drawings, there are no Figures 1, 2, 3 and 9. However, there are Figures 1A-B, 2A-B, 3A-D and 9A-D. Therefore, appropriate reference to the illustrated Figures is required.

Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-8, 12-21 and 25-26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111 (Fed. Cir. 1991), clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" Vas-Cath Inc. v. Mahurkar, 19USPQ2d at 1117. The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." Vas-Cath Inc. v. Mahurkar, 19USPQ2d at 1116.

Applicant's invention is drawn to an antiviral polynucleotide ligand composition and a method of treating viral infection comprising administering a dose of an antiviral polynucleotide composition at a dose sufficient to decrease said viral infection. As defined by the presently claimed invention, an antiviral polynucleotide ligand is a nucleic acid molecule that binds to a virus and acts to decrease the infection of target cells by the virus (page 6, lines 20-21). As such, the instant claims encompass a composition comprising a nucleic acid molecule that binds to any virus via any virus envelope protein or any virus capsid protein (see dependent claim 3) to decrease the infection of target cells by the same virus (an antiviral activity); and a method of treating any viral infection using the same composition. In analyzing whether the required written description is met for genus claims, it is first determined whether a representative number of species has been described by their complete structure. Apart from disclosing 3 distinct RNA polynucleotide ligands L13, L19 and L66 (SEQ ID NOs 2, 12 and 36, respectively; L13 and L66 belong to the non-elected groups of sequences) selected from various distinct groups of RNA ligand sequences listed in Tables 1 & 2, are capable of blocking human

cytomegalovirus (hCMV) entry into targeted cell via their specific binding to hCMV envelope glycoproteins gH, gB and gB, respectively, the instant specification fails to disclose a representative number of polynucleotide ligands that have hCMV antiviral activity via the binding of any hCMV envelope glycoproteins, let alone for polynucleotide ligands having any antiviral activity via the binding of a viral protein other than the hCMV envelope glycoproteins gH and gB. It is further noted that there is no apparent correlation between the ability of an RNA polynucleotide ligand to bind to hCMV and its ability to block hCMV entry into a cell as evidenced by the teachings of the present application for the ligands L17 and L31 (see examples 1 and 2 of the instant specification). Furthermore, Applicants have shown that both L13 and L19 lack an antiviral activity against HSV-1 (top of page 19), and that L66 has no antiviral effect against mouse CMV or HSV-1. As such, apart from the common functional limitation of having antiviral activity, the specification fails to disclose relevant structural characteristics for a representative number of species possessing the desired antiviral activity (e.g., blocking any viral entry via binding any virus protein) within the elected group of antiviral polynucleotide ligand sequences, let alone for a broad antiviral polynucleotide ligand composition as claimed. The claimed invention as a whole is not adequately described if the claims require essential or critical elements which are not adequately described in the claims require essential or critical elements which are not adequately described in the specification and which are not conventional in the art as of Applicants' filing date. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with

sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. Pfaff v. Wells Electronics, Inc., 48 USPQ2d 1641, 1646 (1998). With respect to the elected invention, the skilled artisan cannot envision the detailed structure of a representative number of species having the contemplated antiviral activity other than L19; and a method for treating any viral infection as broadly claimed, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-8, 12-21 and 25-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, with respect to the elected invention while being enabling for

an antiviral polynucleotide ligand composition comprising the polynucleotide sequence set forth in SEQ ID NO:12 and a method of treating hCMV viral infection, said method comprising administering a dose of an antiviral polynucleotide ligand composition comprising the polynucleotide sequence set forth in SEQ ID NO:12 at a dose sufficient to decrease said viral infection, does not reasonably provide enablement for other embodiments of the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The factors to be considered in the determination of an enabling disclosure have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art and the breadth of the claims. *Ex parte Forman*, (230 USPQ 546 (Bd Pat. Appl & Unt, 1986); *In re Wands*, 858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)).

Claims 1-8 and 12-14 are drawn to antiviral polynucleotide ligand composition, the same with the various limitations recited in the dependent claims. Claims 15-21 and 25-26 are directed to a method of treating viral infection, said method comprising administering a dose of an antiviral polynucleotide composition at a dose sufficient to decrease said viral infection, the same method with the various limitations recited in the dependent claims.

The instant specification is not enabled for such a broadly claimed invention for the reasons already set forth in the lack of Written Description above. With the lack of

sufficient guidance provided by the specification, it would have required undue experimentation for a skilled artisan to make and use the instant broadly claimed invention.

With respect to claims 8 and 21 specifically encompassing polynucleotide ligands comprising sequences of SEQ ID NOs. 14-16 having antiviral activity, the instant specification is not enabled for such a claimed invention. This is no evidence of record indicating that polynucleotide ligands having SEQ ID NOs. 14-16 possess any antiviral activity. Although L49 (SEQ ID NO. 16) has extensive homology with L11 (SEQ ID NO. 14) and L58 (SEQ ID NO. 15), and that all of the ligands can bind to hCMV viral paticles, it is unclear whether these ligands are also capable of blocking hCMV entry into a cell by binding to any of its envelope glycoproteins. Moreover, there is no apparent correlation between the ability of an RNA polynucleotide ligand to bind to hCMV and its ability to block hCMV entry into a cell as evidenced by the teachings of the present application for the ligands L17 and L31 (see examples 1 and 2 of the instant specification). Furthermore, the physiological art is recognized as unpredictable (MPEP 2164.03). As set forth in *In re Fisher*, 166 USPQ 18 (CCPA 1970), compliance with 35 USC 112, first paragraph requires:

> That scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the are; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws; in cases involving unpredictagle factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved.

As such, in the absence of sufficient guidance provided by the present disclosure, it would have required undue experimentation for a skilled artisan to make

and use the antiviral polynucleotide ligand composition and a method of treating viral infection as claimed.

Accordingly, due to the lack of guidance provided by the specification regarding to the issues set forth above, the unpredictability of the physiological art and the breadth of the claims, it would have required undue experimentation for one skilled in the art to make and use the instant broadly claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 13-14 and 25-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 13-14 and 25-26 recite the limitation "said polynucleotide ligands" in lines 1 and 2 of the claim. There is insufficient antecedent basis for this limitation in the claim. This is because there is no recitation of polynucleotide ligands in the composition of claims 12 and 1 or in the method of claim 15, respectively.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

The following art rejections are made because the claims read over the teachings of the cited arts for which the instant specification has no written support.

Claims 1-2 and 4-5 are rejected under 35 U.S.C. 102(b) as being anticipated by Pan et al. (Proc. Natl. Acad. Sci. U.S.A. 92: 11509-11513, 1995).

Pan et al. disclose selected pools of RNA and RNA analog (comprising 2'-fluro-2'deoxycytosine and 2'-fluoro-2'deoxyuridine) as well as specific RNA sequences B, C, D and E that have Rous sarcoma virus (RSV)-neutralizing activity (see the entire article, particularly Figs. 3 & 4 and page 11512, col. 2, section titled "Neutralization of RSV by 2'-F-RNA analogs"). This RSV-neutralizing activity is mediated most likely by binding to the virus surface glycoproteins, e.g., gp85 (page 11513, col. 1, first full paragraph).

Accordingly, Pan et al. anticipate the instant claims.

Claims 1-2 and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Ecker et al. (U.S. Patent No. 5,523,389).

Ecker et al. teach compounds comprising a G-quartet structure of phosphorothioate oligonucleotides, each oligonucleotide comprising the sequence TxG4Ty where x and y are independently 0 to 8. The G-quartet structure is found to bind to the HIV envelope protein gp120 at the V3 loop and inhibits both cell to cell and virus to cell infection (see abstract, Summary of the Invention and example 8). Ecker et al. further teach compositions comprising the same compounds in a pharmaceutically acceptable carrier (col. 3, lines 19-23).

Accordingly, Ecker et al. anticipate the instant claims.

Claims 1-2, 4-6, 12-13, 15-19 and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Wang et al. (U.S. Patent No. 5,856,085 with the effective filing date of 12/1/1995).

Wang et al. disclose selected pools of RNA and RNA analog as well as specific RNA sequences B, C, D and E that have Rous sarcoma virus (RSV)-neutralizing activity (see Summary of the invention and examples 8-10). Wang et al. further teach that the nucleic acid analog may comprise substituted nucleotide units such as 2'-amino-2'deoxycytidine or 2'-amino-2'-deoxyuridine residues (col. 3, lines 28-31). The RSV-neutralizing activity is mediated most likely by binding to the virus surface glycoproteins, e.g., gp85 (col. 15, lines 12-30). Wang et al. also teach that the antiviral compounds in a sustained release formulation (biodegradable biopolymers, micelles, gels pr

liposomes; all of which are pharmaceutically acceptable carriers) can be administered into a human or a mammal having the viral infection (col. 9, lines 36-52).

Accordingly, Wang et al. anticipate the instant claims.

Conclusions

Claims 10 and 23 are objected because they are dependent on rejected claims.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (703) 308-8339.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's mentor, Dave Nguyen, may be reached at (703) 305-2024, or SPE, Irem Yucel, Ph.D., at (703) 305-1998.

Any inquiry of a general nature or relating to the status of this application should be directed to Patent Analyst, Tracey Johnson, whose telephone number is (703) 305-2982.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1636.

Quang Nguyen, Ph.D.

DAVE T. NGUYEN
PRIMARY EXAMINER